

Remarks

Claims 31-51 are pending in the subject application. By this Amendment, Applicants have canceled claims 31-51 and added new claims 52-75. Support for the new claims can be found throughout the subject specification and in the claims as originally filed. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 52-75 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

The drawings are objected to under 37 CFR 1.121(d) because Figure 1 is a sequence alignment that is not aligned. By this Amendment, Applicants have replaced the page of the drawings containing Figure 1 to show the proper alignment of the sequence. No new matter has been added. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

The subject specification has been objected to on the grounds that it does not comply with 37 CFR §1.821 through 1.825. Specifically, the specification discloses nucleotide sequences in Figure 1 which are not identified by sequence identifiers. By this Amendment, Applicants have amended the brief description of Figure 1 to include the sequence identifier numbers. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

Claims 31-51 are objected to because of informalities. The Patent Office indicates that claim 31(l) and 31(m) and claim 31(n)(L) and 31(n)(M) comprise the same compositions listed in different orders and that the elements are the same. Applicants respectfully assert that this issue is now moot in view of the cancellation of the previously pending claims. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

The Office Action has indicated that should claims 40 and 42 be found allowable, then claims 41 and 43 will be objected to under 37 CFR 1.75 as being substantial duplicates. As noted above, Applicants have canceled claims 42 and 43 by this Amendment. Accordingly, this rejection is now moot. Reconsideration and withdrawal of the objection is respectfully requested.

Claims 46-51 are rejected under 35 U.S.C. § 112, second paragraph as indefinite. The Office Action indicates that claim 46 recites a method for producing a protein; however, the sole method step is transforming a cell. Applicants respectfully assert that the claims as filed are definite; however, cancellation of claim 46 has rendered this issue moot and reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Claims 46-51 are rejected under 35 U.S.C. § 112, first paragraph, as nonenabled by the subject specification. Applicants respectfully assert that the claims as filed are enabled; however, in view of the cancellation of these claims, it is respectfully submitted that this issue is now moot and reconsideration and withdrawal of the rejection is respectfully requested.

Claims 31-33, 36-38 and 44 are rejected under 35 U.S.C. § 103(a) as obvious over Tuan *et al.* (U.S. Patent No. 6,395,549), Recillas-Targa *et al.* (2002), Chung *et al.* (1997) and Henderson *et al.* (U.S. Patent No. 6,432,700). The Office Action states that Tuan *et al.* teach integrating vectors comprising enhancers, insulators and promoters to drive the expression of any gene of interest in animal cells and to use barrier-function sequences to isolate the integrated vector from position effects in the chromatin to avoid silencing. The Recillas-Targa *et al.* reference is cited as teaching that the position protection effect of the chicken beta-globin insulator is located in a larger region encompassed by SEQ ID NO:1 and is severable from the enhancer blocking activity. In addition, Recillas-Targa *et al.* teach that it is normal to utilize two copies of the position-effect on both sides of the vector that provide for good isolation from position effects. The Office Action indicates that Chung *et al.* teach that the same insulator as Recillas-Targa *et al.* is active in mammalian cells. Finally, the Office Action indicates that Henderson *et al.* teach that is optimal to minimize the size of the other components of the vector, in order to make more room for transgenes which are to be expressed. Applicants respectfully assert that the claimed invention is not obvious over the cited references. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

Claims 31-34, 36-41, 44 and 45 are rejected under 35 U.S.C. § 103(a) as obvious over Tuan *et al.* (U.S. Patent No. 6,395,549, Recillas-Targa *et al.* (2002), Chung *et al.* (1997) and Henderson *et al.* (U.S. Patent No. 6,432,700) and further in view of Perlman *et al.* The Office Action asserts that Perlman *et al.* teach that CHO cells can be used to express FSH from vectors comprising the alpha and beta subunits. Applicants respectfully assert that the claimed invention is not obvious over the cited references. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

Claims 31-33, 35-38 and 44 rejected under 35 U.S.C. § 103(a) as obvious over Tuan *et al.* (U.S. Patent No. 6,395,549, Recillas-Targa *et al.* (2002), Chung *et al.* (1997) and Henderson *et al.*

(U.S. Patent No. 6,432,700) and further in view of Laus *et al.* (U.S. Patent No. 6,194,152). The Office Action claims that Laus *et al.* teach expression of thymidine kinase transgenes as a selectable marker in mammalian cells. Applicants respectfully assert that the claimed invention is not obvious over the cited references. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

Claims 31-33, 36-39 and 42-45 rejected under 35 U.S.C. § 103(a) as obvious over Tuan *et al.* (U.S. Patent No. 6,395,549, Recillas-Targa *et al.* (2002), Chung *et al.* (1997) and Henderson *et al.* (U.S. Patent No. 6,432,700) and further in view of Anderson *et al.* (U.S. Patent No. 6,113,898). The Office Action alleges that Anderson *et al.* teach CHO cells being transformed to express the heavy and light chains of antibodies to the human B7.1 and/or B7.2 antigens. Applicants respectfully assert that the claimed invention is not obvious over the cited references. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

Applicants respectfully submit that one skilled in the art would not have been motivated to have chosen the claimed subsequence of the chicken β -globin insulator for use in vectors in view of the teachings of the cited prior art. For example, Recillas-Targa *et al.* characterize the activity of the chicken β -globin insulator in a chicken cell. It neither teaches nor suggests that 2xcore Δ I-II may be active in cells derived from other species such as cells that are useful for protein production, *e.g.*, CHO cells. Additionally, Recillas-Targa *et al.* teach eleven different constructs comprising the chicken β -globin insulator or fragments thereof (respectively referred to as 1.2 kb insulator, 250-bp, 2xcore, 2x3'HS, 2xcore Δ II, 2x1.2 Δ II, 2xcore Δ I, 2xcore Δ II, 2xcore Δ III, 2xcore Δ IV, 2xcore Δ I-II, see Fig. 1, 2 and 4) and provides no direction, suggestion or incentive to use the 2xcore Δ I-II construct to provide barrier activity such as over the 250-bp core sequence. Indeed, Recillas-Targa *et al.* specifically state: "Our results have the practical consequence of reducing to two copies of the 250-bp core the size of the minimum sequence required for complete barrier action (Fig. 2)" (see page 6888, column 2, last paragraph). Thus, it is respectfully submitted that one skilled in the art would not have looked to fragments smaller than the 250-bp core sequence.

Applicants further submit that the claimed invention provides unexpected results as evidenced by Examples 2 and 3 of the patent application as filed. In these examples, vectors comprising SEQ ID NO: 1 in CHO cells allowed the inventors to obtain (i) more clones expressing

the gene of interest (a five-fold higher probability of identifying clones expressing a gene of interest), and (ii) clones for which the expression levels of a protein of interest are higher. Thus, it is respectfully submitted that the claimed invention is not obvious over the cited combination of references and reconsideration and withdrawal of the rejections of record is respectfully requested.

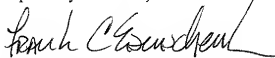
It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



Frank C. Eisenschenk, Ph.D.

Patent Attorney

Registration No. 45,332

Phone No.: 352-375-8100

Fax No.: 352-372-5800

Address: P.O. Box 142950

Gainesville, FL 32614-2950

FCE/sl

Attachment: Replacement Figure 1 (page 1/2)